

## ***Remarks***

### ***I. Support for Amendments***

Support for the foregoing amendments to the claims may be found throughout the specification. Specifically, the amendments to the structure of Formula I in claim 1 have been made to correct obvious chemical errors therein as required by the Examiner in the present Office Action; support for the remaining amendments to claims 1 and 20 may be found at pages 9-10, at page 28, lines 19-24, and in claim 13 as originally filed; support for the amendments to claims 11 and 12 may be found at pages 9 and 23-24; and support for the amendments to claims 22, 23, 25 and 26 may be found at pages 35-40. Accordingly, the present amendments do not add new matter, and their entry is respectfully requested.

### ***II. Status of the Claims***

By the foregoing amendments, claims 13, 14, 16 and 21 have been canceled and claims 1, 11, 12, 15, 20, 22, 23 and 25-28 have been amended. These amendments do not introduce new matter into the application. Upon entry of the foregoing amendments, claims 1-12, 15, 17-20 and 22-29 are pending in the application, with claims 1 and 20 being the independent claims.

### ***III. Summary of the Office Action***

In the Office Action dated October 7, 1999, the Examiner has made four rejections of the claims. Applicants respectfully offer the following remarks to overcome or traverse each of these elements of the Office Action.

***IV. The Rejections Under 35 U.S.C. § 112, Second Paragraph***

In the Office Action at page 2, section 3, the Examiner has rejected claims 1-29 under 35 U.S.C. § 112, second paragraph, as being vague and indefinite. Applicants respectfully traverse this rejection.

***A. The Recitation of "Derivatives Thereof" in Claim 1***

The Examiner first has rejected claims 1-29 for reciting "derivatives thereof," contending that it is unclear what the metes and bounds of "derivatives" are. *See* Office Action at page 2, section 3, lines 2-3. Applicants respectfully disagree with this contention.

In the paragraph bridging pages 24-25, the present specification provides a very detailed description of non-limiting examples of derivatives of compounds of formulae I and II that may be used in accordance with the present invention. Moreover, the specification indicates that these derivatives may be synthesized by one of ordinary skill using routine methods of chemical synthesis. Hence, one of ordinary skill could easily determine the metes and bounds of "derivatives" of the compounds recited in claim 1, in view of the teachings of the present specification. Accordingly, Applicants respectfully assert that claims 1-29 are not indefinite for including the recitation of "derivatives thereof." Reconsideration and withdrawal of this portion of the rejection are therefore respectfully requested.

***B. The Structures of Formulae I and II in Claim 1***

The Examiner next has rejected claims 1-29 for alleged unclarity in the structure of formula I in claim 1. *See* Office Action at page 2, section 3, lines 4-9. Applicants offer the following remarks to traverse and/or accommodate these contentions.

First, Applicants respectfully disagree with the Examiner that it is unclear how the integer a-f recited in Formula I in claim 1 can be more than 1, if for example  $R_3$  is =O or H (*see* Office Action at page 2, section 3, lines 4-5). As claim 1 clearly recites, a, b and c are either 0 or 1, and therefore cannot be more than 1. In contrast, however, claim 1 recites values for the integers d, e and f ranging from 0 to 2, which are permitted since the values for these integers do not depend upon the structure of  $R_3$  in Formula I. Hence, while a determination of whether  $R_3$  is =O or H clearly impacts the permissible values for the integer c in Formula I, this determination has no bearing upon the permissible values for integers d, e and f in Formula I. Accordingly, Applicants respectfully assert that this portion of the rejection is in error; reconsideration and withdrawal are therefore respectfully requested.

Second, by the foregoing amendments, claim 1 has been amended to indicate that if two of  $R_1$ ,  $R_2$  and  $R_3$  are =O, then the other is not =O. Thus, the Examiner's concern that "if  $R_1$ ,  $R_2$ , and  $R_3$  are =O the N can have 6 bonds" (*see* Office Action at page 2, section 3, lines 5-6) has been overcome. In addition, claim 1 has been amended to indicate that the N atom in Formula I is positively charged, thus accommodating the Examiner's requirement in the Office Action at page 2, section 3, lines 6-7.

Finally, the Examiner contends that it is unclear where the bonds crossing the brackets in Formulae I and II should be bonded in the actual formulae inside the brackets. Applicants respectfully disagree with these contentions. One of ordinary skill, reading the formulae recited in claim 1 and using the guidance provided in the specification, for example at pages 18-24, would readily understand that the location of the bonds crossing the brackets in both formulae I and II will depend upon the monomer conformation for each of these formulae. That is, if q is greater than 1 for each of these formulae, then the location of the bond(s) linking the multiple monomers

of formula I to each other, or the multiple monomers of formula II to each other, will depend upon the actual structures chosen from amongst the specific structures recited within claim 1. One of ordinary skill could easily determine the proper location of these bonds, since fundamental rules of chemistry that are well-known in the art will dictate this location depending upon the structures of the monomers. Hence, the fact that the bonds cross the brackets in formulae I and II in claim 1 does not render this claim indefinite, since one of ordinary skill could readily determine the appropriate location of these bonds upon definition of the monomeric subunits using the recitations provided in this claim.

In view of the foregoing remarks, Applicants respectfully assert that the structures recited for formulae I and II in claim 1 do not render this claim, and those that depend therefrom, indefinite. Reconsideration and withdrawal of this portion of the rejection therefore are respectfully requested.

**C.     *The Recitation of Hybridization Conditions in Claims 22-26***

The Examiner next has rejected claims 22-26 contending that these claims are indefinite because it is unclear what the hybridization conditions should be (*i.e.*, low or high stringency). *See* Office Action at page 2, section 3, lines 10-12. Applicants respectfully disagree with these contentions.

Claims 22-26 are drawn to methods for the synthesis, amplification and sequencing of nucleic acid molecules. These methods are described in detail in the specification, for example at pages 34-40 and throughout the Examples at pages 43-53. As one of ordinary skill would appreciate from the claims and the description contained in the specification, particular hybridization conditions (low stringency or high stringency) are not required in order for

operation of the methods as presently claimed. This is because the claims contain functional recitations -- *i.e.*, the mixtures formed in (a) in each of claims 22, 25 and 26 all are incubated in (b) of these claims under conditions whereby nucleic acid molecules are either made (in claims 22 and 23), amplified (in claim 25) or sequenced (in claim 26), *regardless* of the hybridization conditions. As one of ordinary skill would appreciate, nucleic acid molecules may be synthesized, amplified and/or sequenced using low *or* high stringency conditions during the initial hybridization. Although the use of different stringencies may provide different ultimate results, the ability *per se* to synthesize, amplify or sequence from a particular template does not require particular hybridization conditions.

Hence, Applicants respectfully assert that claims 22-26 are not indefinite for lack of recitation of the hybridization conditions used in the claimed methods. Reconsideration and withdrawal of this portion of the rejection are therefore respectfully requested.

***D. The Recitation of "Sufficient" and "Portion" in Claims 22-26***

Finally, the Examiner has rejected claims 22-26 for reciting "sufficient" and "portion," contending that it is unclear what the metes and bounds of these terms are. *See* Office Action at page 2, section 3, lines 12-13. By the foregoing amendments, claims 22, 23, 25 and 26 have been amended to remove the term "sufficient," thereby accommodating this portion of the rejection. Applicants respectfully disagree with the Examiner that the recitation of "a portion" in these claims renders them indefinite. One of ordinary skill in the nucleic acid synthesis, amplification and sequencing arts would readily understand that synthesis, amplification or sequencing of nucleic acid molecules using the methods recited in claims 22-26 will, in many cases, result in the synthesis or amplification of a molecule or population of molecules that is complementary to only

a portion of the input nucleic acid template, rather than to the entire template. In fact, there are many applications wherein amplification or sequencing of *only* a portion of the template is desired, particularly for considerations of efficiency and economy. *See, e.g.,* Mullis *et al.*, U.S. Patent No. 4,800,159 (hereinafter "Mullis;" Doc. "B" listed on the Form PTO-892 attached to Paper No. 5 (referred to hereinafter as "the 892 form")), in Example 1 at col. 20. Therefore, it is irrelevant how long or large the "portion" of the resulting molecule is; so long as the portion is sufficient for use in the particular application for which the nucleic acid molecule is being used, then it can obviously be of any size. Hence, the "metes and bounds" of the "portion" of the template recited in these claims is immaterial, as one of ordinary skill would appreciate. Thus, Applicants respectfully assert that the recitation of "a portion" in claims 22-26 does not render these claims indefinite.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

***E. Summary***

In view of the foregoing remarks, Applicants respectfully assert that the claims as currently presented distinctly claim and particularly point out that which Applicants regard as the invention. Reconsideration and withdrawal of the rejection of claims 1-29 under 35 U.S.C. § 112, second paragraph, are respectfully requested.

***V. The Rejection Under 35 U.S.C. § 102(b) Over Mullis Is Traversed***

In the Office Action at page 3, section 5, the Examiner has rejected claims 20-29 under 35 U.S.C. § 102(b) as being anticipated by Mullis. Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends that:

Mullis *et al.* disclose a method for amplifying any target nucleic acid and a kit. (See abstract and col. 2-5, for example).

Office Action at page 3, section 5, lines 3-4. Applicants respectfully disagree with these contentions.

Claim 20 as originally presented, and as now amended (and hence the remaining claims that depend therefrom) is drawn to a composition comprising, *inter alia*, a component selected from the group consisting of one or more amino acids, one or more saccharides, one or more polyalcohols, and derivatives and combinations thereof. In contrast, Mullis does not disclose compositions comprising one or more of the components recited in the Markush group in claim 20.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Since Mullis fails to expressly or inherently disclose compositions comprising the one or more of the components recited in the Markush group of claim 20, this reference cannot and does not anticipate claims 20-29 as currently presented. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Mullis therefore are respectfully requested.

**VI. The Rejection Under 35 U.S.C. § 102(b) Over Lee Is Traversed**

In the Office Action at page 3, section 6, the Examiner has rejected claims 20-26 under 35 U.S.C. § 102(b) as being anticipated by Lee, U.S. Patent No. 5,187,085 (Doc. "A" listed on the 892 form; hereinafter "Lee"). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends that:

Lee discloses the basic steps of the chain-termination approach to DNA sequencing where the fluorescently labeled chain-terminating nucleotides can be 2', 3', dideoxy-7-deazainosine triphosphate (Col. 3-5).

Office Action at page 3, section 6, lines 3-6. Applicants respectfully disagree with these contentions.

Claim 20 (and hence the remaining claims that depend therefrom) recites compositions comprising, *inter alia*, a component selected from the group consisting of one or more amino acids, one or more saccharides, one or more polyalcohols, and derivatives and combinations thereof. In contrast, Lee only discloses the use of fluorescently labeled chain-terminating nucleotides in the sequencing compositions described therein (*see* Lee at cols. 3-5). Lee does not disclose compositions comprising one or more of the components recited in the Markush group in claim 20.

Since Lee fails to expressly or inherently disclose compositions comprising the one or more of the components recited in the Markush group of claim 20, under *Kalman* this reference cannot and does not anticipate claims 20-29 as currently presented. Reconsideration and withdrawal of this rejection are therefore respectfully requested.

**VII. The Rejection Under 35 U.S.C. § 102(b) Over Solomon Is Traversed**

In the Office Action at page 3, section 7, the Examiner has rejected claims 1-8 under 35 U.S.C. § 102(b) as being anticipated by Solomon, in *Organic Chemistry*, 5th Ed., p. 1094 (1992) (Doc. "U" listed on the 892 form; hereinafter "Solomon"). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends that:



Solomon discloses proline on page [1094] which is viewed as the compound claimed in instant claim 1.

Office Action at page 3, section 7, lines 4-5. Applicants respectfully disagree with these contentions.

Claim 1 as amended (and hence the remaining claims that depend therefrom) recites a composition comprising a compound of Formula II (which may include proline) and at least one enzyme having nucleic acid polymerase activity. In contrast, the relevant disclosure of Solomon is limited to a description of the structure of proline; the reference does not disclose a composition comprising at least one enzyme having nucleic acid polymerase activity.

Thus, Solomon fails to expressly or inherently disclose the composition of claim 1 as amended, and therefore cannot and does not anticipate claims 1-8 as currently presented. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) are therefore respectfully requested.

#### ***VIII. Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this amendment and reply, and allowance of all pending claims, are earnestly solicited.

Respectfully submitted,

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Date: April 6, 2020

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